

=> d his

(FILE 'HOME' ENTERED AT 15:22:04 ON 04 FEB 2004)

FILE 'EUROPATFULL, PATDPAFULL, PCTFULL, RDISCLOSURE, USPATFULL, USPAT2'
ENTERED AT 15:26:38 ON 04 FEB 2004

E METABASIS/PA

L1 32 S E3-E6
L2 2 S L1 AND FBPAASE AND INSULIN(2A)SECRETAGOGUE

FILE 'CAPLUS' ENTERED AT 15:29:58 ON 04 FEB 2004

L3 1 S US6489476/PN
SELECT L3 1 RN
L4 6 S E30-E60

FILE 'REGISTRY' ENTERED AT 15:31:52 ON 04 FEB 2004

L5 1 S 261365-51-9/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 15:32:29 ON 04 FEB 2004

L6 1 S 261365-80-4/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY
L7 11 S E80-E90

FILE 'REGISTRY' ENTERED AT 15:33:01 ON 04 FEB 2004

L8 1 S 261366-05-6/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 15:33:43 ON 04 FEB 2004

L9 1 S 261366-08-9/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY
L10 51 S E300-350

FILE 'REGISTRY' ENTERED AT 15:34:19 ON 04 FEB 2004

L11 1 S 261369-13-5/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY
L12 0 S WO2000038666/PN
L13 0 S WO200038666/PN

FILE 'CAPLUS' ENTERED AT 15:35:47 ON 04 FEB 2004

L14 0 S L12
L15 0 S L13
L16 1 S WO2000038666/PN
SELECT L16 1 RN
L17 4 S E850-E880

FILE 'REGISTRY' ENTERED AT 15:36:56 ON 04 FEB 2004

L18 1 S 261366-99-8/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY
L19 1 S L18

FILE 'CAPLUS' ENTERED AT 15:37:29 ON 04 FEB 2004

L20 4 S L19

FILE 'REGISTRY' ENTERED AT 15:38:57 ON 04 FEB 2004

L21 7 S GLYBURIDE
L22 7 S L21

FILE 'CAPLUS' ENTERED AT 15:54:00 ON 04 FEB 2004

FILE 'REGISTRY' ENTERED AT 15:54:29 ON 04 FEB 2004

L23 1 S 10238-21-8/RN
 SET NOTICE 1 DISPLAY
 SET NOTICE LOGIN DISPLAY

FILE 'REGISTRY' ENTERED AT 15:54:57 ON 04 FEB 2004

 SET TERMSET E#
 DEL SEL Y
 SEL L23 1 RN
L24 1 S E1/RN
 SET TERMSET LOGIN

FILE 'USPATFULL' ENTERED AT 15:55:01 ON 04 FEB 2004

L25 304 S L24
L26 51 S L25 AND PY<=1999 AND (DIABET? OR INSULIN)
L27 881 S GLYBURIDE
L28 714 S L27(S) (DIABET? OR INSULIN)
L29 70 S L28 NOT PY>=1999

FILE 'MEDLINE' ENTERED AT 16:07:27 ON 04 FEB 2004

L30 224 S L29

=> s glyburide
L21 7 GLYBURIDE

=> s l21
L22 7 GLYBURIDE

=> d rn str cn 1-7

L22 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 338752-31-1 REGISTRY

CN Benzamide, 5-chloro-N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, mixt. with N,N-dimethylimidodicarbonimidic diamide monohydrochloride (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

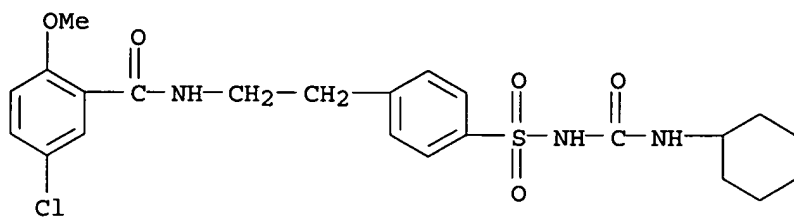
CN Imidodicarbonimidic diamide, N,N-dimethyl-, monohydrochloride, mixt. contg. (9CI)

OTHER NAMES:

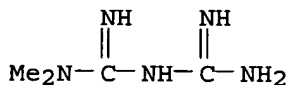
CN Glucovance

CN Glyburide-metformin hydrochloride mixt.

CM 1



CM 2



● HCl

L22 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 338752-30-0 REGISTRY

CN Benzamide, 5-chloro-N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, mixt. with N,N-dimethylimidodicarbonimidic diamide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

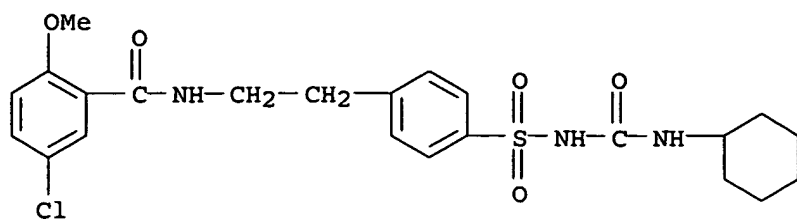
CN Imidodicarbonimidic diamide, N,N-dimethyl-, mixt. contg. (9CI)

OTHER NAMES:

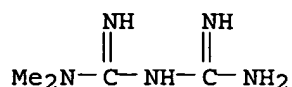
CN Glyburide-metformin mixt.

CM 1

3/8/50

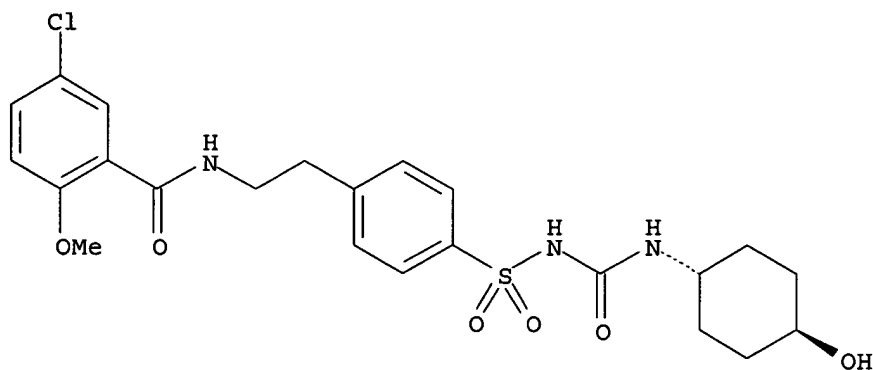


CM 2



L22 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 23155-00-2 REGISTRY

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzamide, 5-chloro-N-[2-[4-[[[(trans-4-hydroxycyclohexyl)amino]carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzamide, 5-chloro-N-[2-[4-[[[(4-hydroxycyclohexyl)amino]carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, trans-

CN Urea, 1-[p-[2-(5-chloro-o-anisamido)ethyl]phenyl]sulfonyl]-3-(4-hydroxycyclohexyl)-, trans- (8CI)

OTHER NAMES:

CN 4-trans-Hydroxyglibenclamide

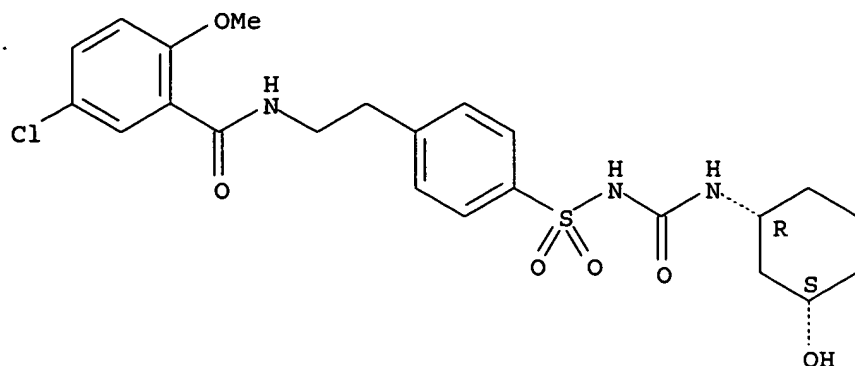
CN N-[4-[.beta.-(2-Methoxy-5-chlorobenzamido)ethyl]benzenesulfonyl]-N'-(trans-4-hydroxycyclohexyl)urea

CN **trans-4-Hydroxyglyburide**

CN trans-N-4-[2-(5-Chloro-2-methoxybenzamido)ethyl]phenylsulfonyl-N'-(4-hydroxycyclohexyl)urea

L22 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 23074-02-4 REGISTRY

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzamide, 5-chloro-N-[2-[4-[[[(1R,3S)-3-hydroxycyclohexyl]amino]carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzamide, 5-chloro-N-[2-[4-[[[(3-hydroxycyclohexyl)amino]carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, cis-

CN Urea, 1-[[p-[2-(5-chloro-o-anisamido)ethyl]phenyl]sulfonyl]-3-(3-hydroxycyclohexyl)-, cis- (8CI)

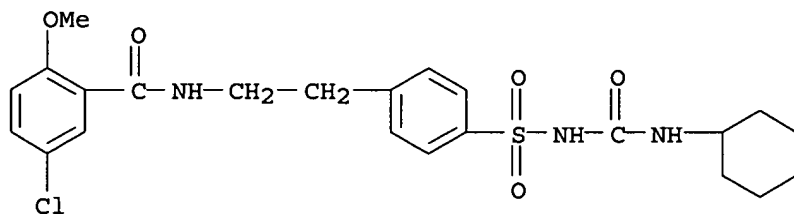
OTHER NAMES:

CN 3-cis-Hydroxyglybenclamide

CN **cis-3-Hydroxyglyburide**

L22 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 23047-14-5 REGISTRY



● x K

CN Benzamide, 5-chloro-N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy-, potassium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, 1-[[p-[2-(5-chloro-o-anisamido)ethyl]phenyl]sulfonyl]-3-cyclohexyl-, potassium salt (8CI)

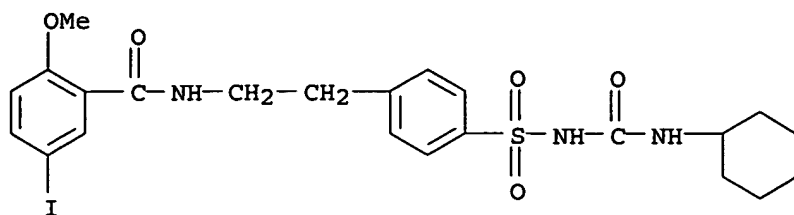
OTHER NAMES:

CN **Glyburide, potassium salt**

CN Potassium N-[4-[2-(5-chloro-2-methoxybenzamido)ethyl]phenylsulfonyl]-N'-cyclohexylurea

L22 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 16789-77-8 REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzamide, N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-5-iodo-2-methoxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Urea, 1-cyclohexyl-3-[p-[2-(5-iodo-o-anisamido)ethyl]phenyl]sulfonyl] - (8CI)

OTHER NAMES:

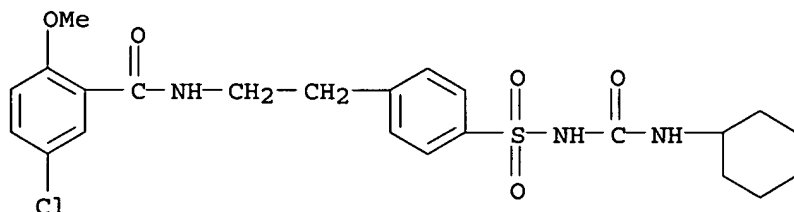
CN Iodoglibenclamide

CN Iodoglyburide

CN LY 285110

L22 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN

RN 10238-21-8 REGISTRY



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

CN Benzamide, 5-chloro-N-[2-[4-[[[(cyclohexylamino)carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-[4-[2-(5-Chloro-2-methoxybenzamido)ethyl]phenylsulfonyl]-3-cyclohexylurea

CN 1-[p-2-(5-Chloro-o-anisamido)ethylphenylsulfonyl]-3-cyclohexylurea

CN 1-[[p-[2-(5-Chloro-o-anisamido)ethyl]phenyl]sulfonyl]-3-cyclohexylurea

CN Abbenclamide

CN Adiab

CN Antibet

CN Apo-Glibenclamide

CN Azuglucon

CN Bastiverit

CN Benclamin

CN Betanase

CN Betanaz

CN Betanese 5

CN Calabren

CN Cytagon

CN Daonil

CN Daonil N

CN Debtan

CN Dia-basan
CN Diaben
CN Diabeta
CN Diabiphage
CN Dibelet
CN Duraglucon
CN Euglucon
CN Euglucon
CN Euglucon 5
CN Euglykon
CN GBN 5
CN Gilemal
CN Gl
CN Glamide
CN Gliban
CN Gliben
CN Gliben-Puren N
CN Glibenclamide
CN Glibenil
CN Glibens
CN Glibesyn
CN Glibet
CN Glibetic
CN Glibil
CN Gliboral
CN Glicem
CN Glidiabet
CN Glimel
CN Glimide
CN Glimidstada
CN Glisulin
CN Glitisol
CN Glyburide

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
DISPLAY

Inventor

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FILE 'USPAT2' ENTERED AT 15:26:38 ON 04 FEB 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> e metabasis/pa

E1	3	METAALWERKEN/PA
E2	1	METAB/PA
E3	32 -->	METABASIS/PA
E4	13	METABASIS THERAPEUTICS INC/PA
E5	2	METABASIS THERAPEUTICS INC., SAN DIEGO, CALIF., US/PA
E6	12	METABASIS THERAPEUTICS, INC./PA
E7	6	METABIO/PA
E8	3	METABIO JOULLIE/PA
E9	1	METABIO-JOULLIE, NEUILLY-SUR-SEINE, FR/PA
E10	6	METABION/PA
E11	1	METABION GESELLSCHAFT FUER ANGEWANDTE BIOTECHNOLOGIE/PA
E12	1	METABION GESELLSCHAFT FUR ANGEWANDTE BIOTECHNOLOGIE MBH/PA

=> s e3-e6

L1 32 (METABASIS/PA OR "METABASIS THERAPEUTICS INC"/PA OR "METABASIS THERAPEUTICS INC., SAN DIEGO, CALIF., US"/PA OR "METABASIS THERAPEUTICS, INC. "/PA)

=> s l1 and fbpase and insulin(2a)secretagogue

L2 2 L1 AND FBPASE AND INSULIN(2A) SECRETAGOGUE

=> d ibib 1-2

L2 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2002003978 PCTFULL ED 20020814
TITLE (ENGLISH): A COMBINATION OF **FBPase** INHIBITORS AND
ANTIDIABETIC AGENTS USEFUL FOR THE TREATMENT OF
DIABETES
TITLE (FRENCH): COMBINAISON D'INHIBITEURS DE **FBPASE** ET
D'AGENTS ANTIDIABETIQUES UTILE POUR LE TRAITEMENT DU
DIABETE
INVENTOR(S): VAN POELJE, Paul, D.;
ERION, Mark, D.;
FUJIWARA, Toshihiko
PATENT ASSIGNEE(S): **METABASIS THERAPEUTICS, INC.**;
SANKYO COMPANY, LIMITED;
VAN POELJE, Paul, D.;
ERION, Mark, D.;
FUJIWARA, Toshihiko
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE

WO 2002003978	A2	20020117

07/900, 364

L30 ANSWER 30 OF 224 MEDLINE on STN
ACCESSION NUMBER: 96431984 MEDLINE
DOCUMENT NUMBER: 96431984 PubMed ID: 8835050
TITLE: Metformin: an antihyperglycemic agent for treatment of type II diabetes.
AUTHOR: Melchior W R; Jaber L A
CORPORATE SOURCE: Drug Information, St. Joseph Mercy Hospital, Pontiac, MI, USA.
SOURCE: ANNALS OF PHARMACOTHERAPY, (1996 Feb) 30 (2) 158-64. Ref: 48
Journal code: 9203131. ISSN: 1060-0280.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19961219
Entered Medline: 19961127

AB OBJECTIVE: To review the comparative efficacy of metformin, sulfonylureas, and insulin in the treatment of patients with type II diabetes. DATA SOURCES: Articles were identified by a MEDLINE search of articles from 1966 to 1994, using the terms metformin, sulfonylurea, chlorpropamide, glipizide, glyburide, tolazamide, tolbutamide, and insulin, published in English, French, or German. Articles also were identified from bibliographies of pertinent articles. STUDY SELECTION: With the exception of articles dealing with the pharmacology of metformin, only randomized, active, controlled studies were selected for review. DATA EXTRACTION: Effects of metformin therapy on metabolic and cardiovascular risk factors were abstracted: weight, blood pressure, total and low-density lipoprotein cholesterol, triglycerides, fasting and postprandial glucose, and glycosylated hemoglobin. DATA SYNTHESIS: Metformin is an antihyperglycemic agent with a mean bioavailability of 50-60%. It is eliminated primarily by renal filtration and secretion and has a half-life of approximately 6 hours in patients with type II diabetes. Although the half-life of metformin is prolonged in patients with renal impairment, no specific dosage adjustments have been recommended. This agent has no effect in the absence of insulin. Metformin is as effective as the sulfonylureas in treating patients with type II diabetes and has a more prominent postprandial effect than the sulfonylureas or insulin. When combined with a sulfonylurea, metformin has been shown to exert antihyperglycemic effects in addition to the sulfonylurea with which it is combined. Metformin decreases absorption of vitamin B12 and folic acid, although reported cases of megaloblastic anemia are rare. Cimetidine decreases the elimination of metformin; therefore, the manufacturer recommends a reduced metformin dosage when these agents are combined. The most frequently reported adverse effects of metformin are gastrointestinal in nature (diarrhea, nausea, abdominal pain, and metallic taste, in decreasing order). Metformin has been used in Canada, Great Britain, and the rest of Europe for more than 30 years and was approved for use in the US in December 1994. CONCLUSIONS: Three trials comprise the Food and Drug Administration approval database (one foreign). Metformin will be most useful in managing patients with poorly controlled postprandial hyperglycemia, as its postprandial effect is much greater than that of the sulfonylureas. In contrast, sulfonylureas or insulin are more effective for managing patients with poorly controlled fasting hyperglycemia. Metformin should be considered a first-line agent, particularly in obese or hyperlipidemic patients.